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INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)



Applicant's or agent's file reference 10294-WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/DK 03/00198	International filing date (day/month/year) 25.03.2003	Priority date (day/month/year) 10.04.2002
International Patent Classification (IPC) or both national classification and IPC C12N15/75		
Applicant NOVOZYMES AS et al.		

- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

 These annexes consist of a total of sheets.

- This report contains indications relating to the following items:
 - ☒ Basis of the opinion
 - ☐ Priority
 - ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - ☒ Lack of unity of invention
 - ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - ☐ Certain documents cited
 - ☐ Certain defects in the international application
 - ☐ Certain observations on the international application

Date of submission of the demand 31.10.2003	Date of completion of this report 30.07.2004
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer van Heusden, M Telephone No. +49 89 2399-8145 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/DK 03/00198

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-15 as originally filed

Claims, Numbers

1-22 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
 - ☐ the language of publication of the international application (under Rule 48.3(b)).
 - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:
- ☒ contained in the international application in written form.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority in written form.
 - ☐ furnished subsequently to this Authority in computer readable form.
 - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.
4. The amendments have resulted in the cancellation of:
- ☐ the description, pages:
 - ☐ the claims, Nos.:
 - ☐ the drawings, sheets:
5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
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IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees, the applicant has:

- ☐ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☐ all parts.
- ☒ the parts relating to claims Nos. partially claims 1-22, insofar as they relate to SEQ ID NO: 133 and 134 .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-22
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-22
Industrial applicability (IA)	Yes: Claims	1-22
	No: Claims	

2. Citations and explanations

see separate sheet

Additional remarks to section IV:

The IPEA agrees with the ISA in that the present application lacks unity, for the reasons as presented by the ISA. The search report has been made up for the two groups of inventions relating to SEQ ID NO: 2 and 134. The applicant has requested detailed substantive examination of the second group of inventions, relating to SEQ ID NO: 134. Thus this written opinion concerns claims 1-22 insofar as they relate to SEQ ID NO: 134.

Additional remarks to section V:

1. Novelty (Article 33(2) PCT)

- 1.1 The present application discloses a *Bacillus licheniformis* mutant host cell which is mutated in the gene encoding a polypeptide which is at least 80% identical to SEQ ID NO: 134 and which mutated host cell secretes at least 5% less of said polypeptide than the parent host cell under comparable cultivation conditions. It further relates to a process of producing a product of interest using said mutant *B. licheniformis*.
- 1.2 The documents mentioned in this report are numbered as in the International Search Report (ISR), i.e. D1 corresponds to the first document of the ISR etc.
- 1.3 None of the cited prior art documents discloses a polypeptide represented by SEQ ID NO: 134 nor any polypeptide being 80% identical thereto. Therefore the subject matter of claims 1-22 can be considered novel.

2. Inventive step (Article 33(3) PCT)

- 2.1 The present application does not seem to satisfy the criterion set forth in Article 33(3) PCT because the subject matter of claims 1-22 does not involve an inventive step in view of documents D1-D3 and D5-D7, which all relate to mutant *Bacillus* species (especially *B. licheniformis*) in which extracellular proteases are mutated to improve the production of heterologous products by said *Bacillus* hosts.

The present application differs from the disclosure in said documents in that a further gene encoding a further extracellular protein (with unknown function) is mutated, resulting in improved production of a heterologous product from said *B.*

licheniformis host. Therefore the objective problem to be solved by the present application can be seen as the provision of a further B. licheniformis mutant for the production of a heterologous product.

The solution provided, the mutant in which the gene encoding the polypeptide represented by SEQ ID NO: 134 is mutated, appears to be an arbitrary selection among many possible secreted proteins of the host cell. Said selection, being arbitrary, is not considered to involve an inventive step. Inventive step could be recognized only if said mutant shows some unexpected advantage. In this respect, it seems that the specific mutant of the example (relating to SEQ ID NO: 134) was not shown to provide any advantageous effect. The application lacks any disclosure on improved purification conditions of a heterologous product of interest when expressed in said mutant.

- 2.2 The applicant has defined the problem to be solved on p. 1 of the description as the reduction of necessary product purification when producing a product of interest in the host cell. This, however, seems to be the result that is achieved. Moreover, this feature is inherent in any of documents D1-D3 or D5-D7: for instance in D1 the proteases are virtually eliminated thus inherently implying a reduction in the amount of secreted polypeptide of at least 5%. It seems that this will result in a reduction of necessary product purification.

3. Industrial applicability (Article 33(4) PCT)

The subject matter of claims 1-22 appears to be industrially applicable.